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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 27	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28	Oct 21	EVENTLINE has been reloaded
NEWS 29	Oct 24	BEILSTEIN adds new search fields
NEWS 30	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 32	Nov 18	DKILIT has been renamed APOLLIT
NEWS 33	Nov 25	More calculated properties added to REGISTRY
NEWS 34	Dec 02	TIBKAT will be removed from STN
NEWS 35	Dec 04	CSA files on STN

NEWS EXPRESS	October 14 CURRENT WINDOWS VERSION IS V6.01, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 14:32:38 ON 11 DEC 2002

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:32:46 ON 11 DEC 2002
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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STRUCTURE FILE UPDATES: 10 DEC 2002 HIGHEST RN 475623-85-9
DICTIONARY FILE UPDATES: 10 DEC 2002 HIGHEST RN 475623-85-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

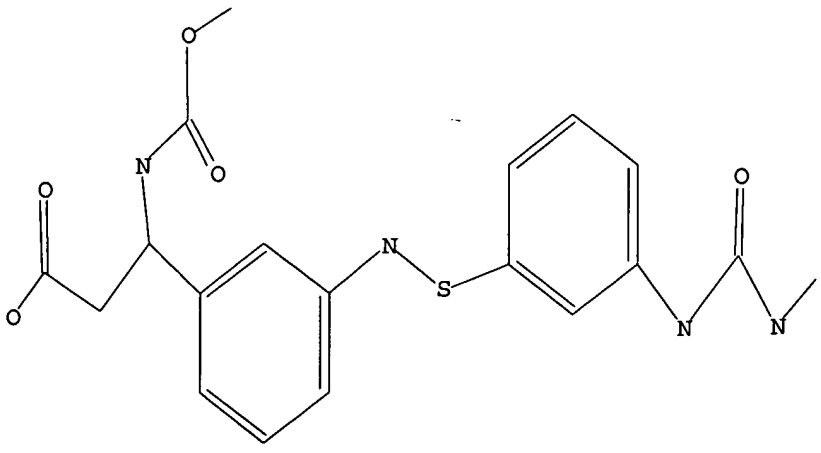
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09889455.str

L1 STRUCTURE UPLOADED

=> d query
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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=> s l1
SAMPLE SEARCH INITIATED 14:33:13 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      5 TO ITERATE

100.0% PROCESSED       5 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            5 TO      234
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 14:33:18 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    180 TO ITERATE

100.0% PROCESSED     180 ITERATIONS                               7 ANSWERS
SEARCH TIME: 00.00.01

L3            7 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   140.28     140.49

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FILE COVERS 1907 - 11 Dec 2002  VOL 137 ISS 24
FILE LAST UPDATED: 10 Dec 2002  (20021210/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> s l3
L4            3 L3

=> d l4 1-3 abs ibib hitstr
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L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS

AB The present invention relates to cytostatics which have a tumor-specific action as a result of linkage to .alpha.v.beta.3 integrin antagonists via preferred linking units which can be selectively cleaved by elastase, i.e. by an enzyme which can esp. be found in tumor tissue. The preferred linking units provide sufficient stability of the conjugate of cytostatic and .alpha.v.beta.3 integrin antagonist in biol. fluids and, at the same time, the desired intracellular action within tumor cells as a result of its specific enzymic or hydrolytic cleavability with release of the cytostatic.

ACCESSION NUMBER: 2002:693123 CAPLUS
DOCUMENT NUMBER: 137:210930
TITLE: Enzyme-activated cytostatic conjugates with integrin ligands
INVENTOR(S): Lerchen, Hans-georg; Baumgarten, Joerg; Schoop, Andreas; Albers, Markus
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 72 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

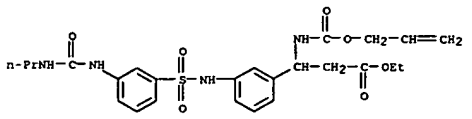
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1238678	A1	20020911	EP 2001-105350	20010308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002072151	A1	20020919	WO 2002-EP2501	20020307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2001-105350 A 20010308
OTHER SOURCE(S): MARPAT 137:210930

IT **455941-30-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enzyme-activated cytostatic conjugates with integrin ligands which can be selectively cleaved by elastase in relation to toxicity to hemopoietic stem cells)

RN 455941-30-7 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2-propenyloxy)carbonyl]amino]-3-[[[3-[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS

AB The invention relates to cytostatics CT-LI-Sp-IA [CT denotes a cytotoxic radical or a radical of a cytostatic or a cytostatic deriv. which can addnl. carry a hydroxy, carboxy or amino group; LI is a linker group comprising 5- to 8-amino acid residues in the D- or L-configuration, which can each optionally carry protective groups; Sp is absent or a carbonyl or thiocarbonyl radical; IA is a non-peptide radical addressing an .alpha.v.beta.3 integrin receptor, e.g., a radical of formula R18COCH2CHPhNHCOCH2NHCO-m-C6H4NH[C(:NH)NHR19]q, where R18 is OH, (un)substituted (cyclo)alkoxy, aryloxy, heterocyclyloxy, a direct bond, or an atom from the group N, O and S, via which the radical is bonded to the rest of the conjugate; q is 0 or 1; R19 is H, (un)substituted (cyclo)alkyl, aryl, heterocyclyl, an alkylamine or alkylamide radical, or a direct bond, via which the radical is bonded to the rest of the conjugate] and their physiol. acceptable salts and stereoisomers. The cytostatics have a tumor-specific action as a result of linkage to .alpha.v.beta.3integrin antagonists via preferred linking units which can be selectively cleaved by enzymes such as metallo matrix proteases (MMPs5), i.e., by enzymes which can esp. be found in tumor tissue. The preferred linking units guarantee the serum stability of the conjugate of cytostatic and .alpha.v.beta.3 integrin antagonist and, at the same time, the desired intracellular action within tumor cells as a result of its specific enzymic or hydrolytic cleavability with release of the cytostatic. Thus, 20-O-[PrNHCONH-m-C6H4SO2NH-m-C6H4CH(CH2CO2H)NHCONH-p-C6H4NHC(S)-Pro-Leu-Gly-Leu-His-Val]camptothecin (1) was prepd. by reaction of 20(S)-camptothecin with N-(tert-butoxycarbonyl)-L-valine-N-carboxyanhydride, deprotection, peptide coupling reactions, and formation of the thiourea linkage. Compd. 1 was assayed for cytostatic action on human large intestine cell line HT29 (IC50 = 40 nM).

ACCESSION NUMBER: 2002:503334 CAPLUS
DOCUMENT NUMBER: 137:63479
TITLE: Preparation of conjugates of integrin receptor antagonists and a cytostatic agent having specifically cleavable linking units
INVENTOR(S): Lerchen, Hans-Georg; Baumgarten, Joerg; Lockhoff, Oswald; Albers, Markus; Schoop, Andreas
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 127 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

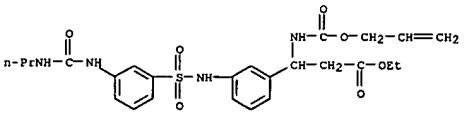
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1219305	A1	20020703	EP 2000-128401	20001227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002051444	A1	20020704	WO 2001-EP14965	20011218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002183256	A1	20021205	US 2001-26408	20011221

PRIORITY APPLN. INFO.: EP 2000-128401 A 20001227
OTHER SOURCE(S): MARPAT 137:63479

IT **439865-63-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of conjugates of integrin receptor antagonists and a cytostatic agent having specifically cleavable linking units)

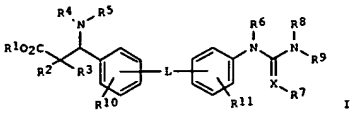
RN 439865-63-1 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2-propenyloxy)carbonyl]amino]-3-[[[3-[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
GI



I

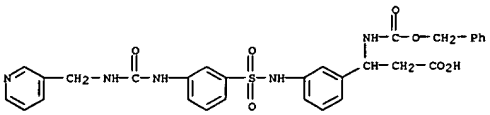
AB .beta.-Phenylalanine derivs. I [R1 = H, (un)substituted alkyl, cycloalkyl, aryl, heterocyclyl; R2, R3 = any group given for R1 or (un)substituted alkenyl or alkynyl, OH, alkoxy or R2 and R3 are bonded to each other; R4 = carboxy ester, SO2H, CHO, CONH2, C(S)NH2 or their derivs.; R5 = H, (un)substituted alkyl, cycloalkyl, aryl; R6 = any group given for R1 or is bonded to one of R7, R8 or R9; R7 is absent, H, (un)substituted alkyl or cycloalkyl, NO2, CN, CHO or CO2H or their derivs., or is bonded to one of R6, R8, or R9; R8, R9 = any group given for R1 or is bonded to one of R6, R7 or R9 or R8; R10, R11 = H, (un)substituted alkyl, cycloalkyl, or alkoxy, halo; L is a sulfonamide, amide, ether, ester, keto, urea, thioether, sulfoxide or sulfone unit optionally extended by one or two methylene groups; X is N, O or S] and their physiol. acceptable salts and stereoisomers were prepd. Thus, 3-[(phenylsulfonyl)amino]-3-[3-[(3-guanidinophenyl)sulfonyl]phenyl]propionic acid trifluoroacetic acid salt, prepd. by a multistep procedure from 3-nitrobenzaldehyde, ammonium acetate, malonic acid, benzenesulfonyl chloride, 3-nitrobenzenesulfonyl chloride, and 1,3-bis(tert-butoxycarbonyl)-2-methyl-2-thiopseudourea, showed IC50 = 19 nM antagonist activity against integrin .alpha.v.beta.3 receptor.

ACCESSION NUMBER: 2000:493269 CAPLUS
DOCUMENT NUMBER: 133:105343
TITLE: Preparation of .beta.-phenylalanine derivatives as integrin antagonists
INVENTOR(S): Schoop, Andreas; Muller, Gerhard; Bruggemeier, Ulf; Schmidt, Delf; Stelte-Ludwig, Beatrix; Keldenich, Jorg; Albers, Markus
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

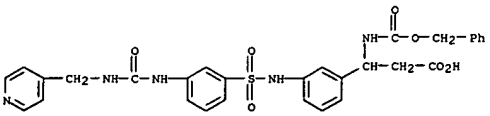
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000041469	A2	20000720	WO 2000-EP120	20000111
WO 2000041469	A3	20001116		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,

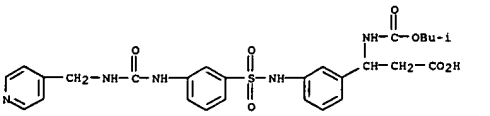
L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS (Continued)



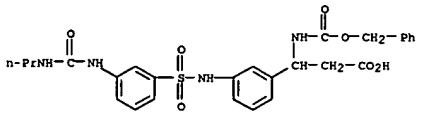
RN 283612-99-7 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(phenylmethoxy)carbonyl]amino]-3-[[[3-[[[(4-pyridinylmethyl)amino]carbonyl]amino]phenyl]sulfonyl]amino]- (9CI) (CA INDEX NAME)



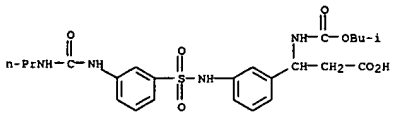
RN 283613-01-4 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2-methylpropoxy)carbonyl]amino]-3-[[[3-[[[(4-pyridinylmethyl)amino]carbonyl]amino]phenyl]sulfonyl]amino]- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS (Continued)
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 6291503 B1 20010918 US 1999-232738 19990115
EP 1147079 A2 20011024 EP 2000-903571 20000111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002534439 T2 20021015 JP 2000-593094 20000111
US 2001031788 A1 20011018 US 2001-867835 20010530
PRIORITY APPLN. INFO.: US 1999-232738 A 19990115
WO 2000-EP120 W 20000111
OTHER SOURCE(S): MARPAT 133:105343
IT **283612-93-1P 283612-94-2P 283612-98-6P**
283612-99-7P 283613-01-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .beta.-phenylalanine derivs. as integrin antagonists)
RN 283612-93-1 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(phenylmethoxy)carbonyl]amino]-3-[[[3-[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]- (9CI) (CA INDEX NAME)



RN 283612-94-2 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2-methylpropoxy)carbonyl]amino]-3-[[[3-[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]- (9CI) (CA INDEX NAME)



RN 283612-98-6 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(phenylmethoxy)carbonyl]amino]-3-[[[3-[[[(3-pyridinylmethyl)amino]carbonyl]amino]phenyl]sulfonyl]amino]- (9CI) (CA INDEX NAME)

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	15.94	156.43

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.86	-1.86

FILE 'REGISTRY' ENTERED AT 14:37:16 ON 11 DEC 2002

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 DEC 2002 HIGHEST RN 475623-85-9
DICTIONARY FILE UPDATES: 10 DEC 2002 HIGHEST RN 475623-85-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

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SAMPLE SCREEN SEARCH COMPLETED -      3 TO ITERATE

100.0% PROCESSED       3 ITERATIONS                              3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            3 TO      163
PROJECTED ANSWERS:               3 TO      163

L6            3 SEA SSS SAM L5

=> s l5 full
FULL SEARCH INITIATED 14:43:33 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    128 TO ITERATE

100.0% PROCESSED     128 ITERATIONS                           116 ANSWERS
SEARCH TIME: 00.00.01

L7          116 SEA SSS FUL L5

=> fil caplus
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                 144.08     300.51

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                     ENTRY    SESSION
CA SUBSCRIBER PRICE                                   0.00      -1.86
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=> d l8 abs ibib

L8 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS

AB The present invention relates to cytostatics which have a tumor-specific action as a result of linkage to .alpha.v.beta.3 integrin antagonists via preferred linking units which can be selectively cleaved by elastase, i.e. by an enzyme which can esp. be found in tumor tissue. The preferred linking units provide sufficient stability of the conjugate of cytostatic and .alpha.v.beta.3 integrin antagonist in biol. fluids and, at the same time, the desired intracellular action within tumor cells as a result of its specific enzymic or hydrolytic cleavability with release of the cytostatic.

ACCESSION NUMBER: 2002:693123 CAPLUS
DOCUMENT NUMBER: 137:210930
TITLE: Enzyme-activated cytostatic conjugates with integrin ligands
INVENTOR(S): Lerchen, Hans-georg; Baumgarten, Joerg; Schoop, Andreas; Albers, Markus
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 72 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1238678	A1	20020911	EP 2001-105350	20010308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002072151	A1	20020919	WO 2002-EP2501	20020307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2001-105350 A 20010308
OTHER SOURCE(S): MARPAT 137:210930
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d l8 2-4 abs ibib
```

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS

AB The invention relates to cytostatics CT-LI-Sp-IA [CT denotes a cytotoxic radical or a radical of a cytostatic or a cytostatic deriv. which can addnl. carry a hydroxy, carboxy or amino group; LI is a linker group comprising 5- to 8-amino acid residues in the D- or L-configuration, which can each optionally carry protective groups; Sp is absent or a carbonyl or thiocarbonyl radical; IA is a non-peptide radical addressing an .alpha.v.beta.3 integrin receptor, e.g., a radical of formula R18COCH2CHPhNHCOCH2NHCO-m-C6H4NH[C(:NH)NHR19]q, where R18 is OH, (un)substituted (cyclo)alkoxy, aryloxy, heterocyclyloxy, a direct bond, or an atom from the group N, O and S, via which the radical is bonded to the rest of the conjugate; q is 0 or 1; R19 is H, (un)substituted (cyclo)alkyl, aryl, heterocyclyl, an alkylamine or alkylamide radical, or a direct bond, via which the radical is bonded to the rest of the conjugate] and their physiol. acceptable salts and stereoisomers. The cytostatics have a tumor-specific action as a result of linkage to .alpha.v.beta.3integrin antagonists via preferred linking units which can be selectively cleaved by enzymes such as metallo matrix proteases (MMPs5), i.e., by enzymes which can esp. be found in tumor tissue. The preferred linking units guarantee the serum stability of the conjugate of cytostatic and .alpha.v.beta.3 integrin antagonist and, at the same time, the desired intracellular action within tumor cells as a result of its specific enzymic or hydrolytic cleavability with release of the cytostatic. Thus, 20-O-[PrNHCONH-m-C6H4SO2NH-m-C6H4CH(CH2CO2H)NHCONH-p-C6H4NHC(S)-Pro-Leu-Gly-Leu-His-Val]camptothecin (1) was prepd. by reaction of 20(S)-camptothecin with N-(tert-butoxycarbonyl)-L-valine-N-carboxyanhydride, deprotection, peptide coupling reactions, and formation of the thiourea linkage. Compd. 1 was assayed for cytostatic action on human large intestine cell line HT29 (IC50 = 40 nM).

ACCESSION NUMBER: 2002:503334 CAPLUS
DOCUMENT NUMBER: 137:63479
TITLE: Preparation of conjugates of integrin receptor antagonists and a cytostatic agent having specifically cleavable linking units
INVENTOR(S): Lerchen, Hans-Georg; Baumgarten, Joerg; Lockhoff, Oswald; Albers, Markus; Schoop, Andreas
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 127 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

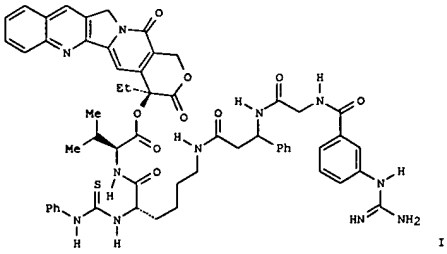
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1219305	A1	20020703	EP 2000-128401	20001227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002051444	A1	20020704	WO 2001-EP14965	20011218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,				

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS (Continued)

TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002183256 A1 20021205 US 2001-26408 20011221
PRIORITY APPLN. INFO.: EP 2000-128401 A 20001227
OTHER SOURCE(S): MARPAT 137:63479
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS

GI



I

AB Title compds., e.g., I, cytostatics which have a tumor-specific action as a result of linkage to .alpha.V.beta.3 integrin ligands, were prepd.. Data for biol. activity of title compds. were given.

ACCESSION NUMBER: 2001:185604 CAPLUS
DOCUMENT NUMBER: 134:237346
TITLE: Preparation of peptidyl camptothecin conjugates as antitumor agents
INVENTOR(S): Lerchen, Hans-Georg; Baumgarten, Joerg; Brueggemeier, Ulf; Albers, Markus; Schoop, Andreas; Schulze, Thomas
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 239 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

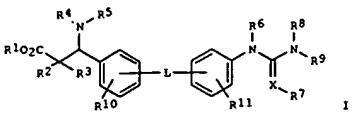
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001017563	A2	20010315	WO 2000-EP8361	20000828
WO 2001017563	A3	20020711		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000013883	A	20020507	BR 2000-13883	20000828
EP 1235595	A2	20020904	EP 2000-965901	20000828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-392167 A 19990908
US 2000-606772 A 20000629

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS (Continued)

WO 2000-EP8361 W 20000828
OTHER SOURCE(S): MARPAT 134:237346

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS
GI



I

AB .beta.-Phenylalanine derivs. I [R1 = H, (un)substituted alkyl, cycloalkyl, aryl, heterocyclyl; R2, R3 = any group given for R1 or (un)substituted alkenyl or alkynyl, OH, alkoxy or R2 and R3 are bonded to each other; R4 = carboxy ester, SO2H, CHO, CONH2, C(S)NH2 or their derivs.; R5 = H, (un)substituted alkyl, cycloalkyl, aryl; R6 = any group given for R1 or is bonded to one of R7, R8 or R9; R7 is absent, H, (un)substituted alkyl or cycloalkyl, NO2, CN, CHO or CO2H or their derivs., or is bonded to one of R6, R8, or R9; R8, R9 = any group given for R1 or is bonded to one of R6, R7 or R9 or R8; R10, R11 = H, (un)substituted alkyl, cycloalkyl, or alkoxy, halo; L is a sulfonamide, amide, ether, ester, keto, urea, thioether, sulfoxide or sulfone unit optionally extended by one or two methylene groups; X is N, O or S] and their physiol. acceptable salts and stereoisomers were prepd. Thus, 3-[(phenylsulfonyl)amino]-3-[3-[(3-guanidinophenyl)sulfonyl]phenyl]propionic acid trifluoroacetic acid salt, prepd. by a multistep procedure from 3-nitrobenzaldehyde, ammonium acetate, malonic acid, benzenesulfonyl chloride, 3-nitrobenzenesulfonyl chloride, and 1,3-bis(tert-butoxycarbonyl)-2-methyl-2-thiopseudourea, showed IC50 = 19 nM antagonist activity against integrin .alpha.v.beta.3 receptor.

ACCESSION NUMBER: 2000:493269 CAPLUS
DOCUMENT NUMBER: 133:105343
TITLE: Preparation of .beta.-phenylalanine derivatives as integrin antagonists
INVENTOR(S): Schoop, Andreas; Muller, Gerhard; Bruggemeier, Ulf; Schmidt, Delf; Stelte-Ludwig, Beatrix; Keldenich, Jorg; Albers, Markus
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000041469	A2	20000720	WO 2000-EP120	20000111
WO 2000041469	A3	20001116		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS (Continued)
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6291503	B1	20010918	US 1999-232738	19990115
EP 1147079	A2	20011024	EP 2000-903571	20000111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002534439	T2	20021015	JP 2000-593094	20000111
US 2001031788	A1	20011018	US 2001-867835	20010530
PRIORITY APPLN. INFO.:			US 1999-232738 A	19990115
			WO 2000-EP120 W	20000111

OTHER SOURCE(S): MARPAT 133:105343

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     FILE 'REGISTRY' ENTERED AT 14:32:46 ON 11 DEC 2002
L1             STRUCTURE UPLOADED
L2           0 S L1
L3           7 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 14:33:21 ON 11 DEC 2002
L4           3 S L3

     FILE 'REGISTRY' ENTERED AT 14:37:16 ON 11 DEC 2002
L5             STRUCTURE UPLOADED
L6           3 S L5
L7         116 S L5 FULL

     FILE 'CAPLUS' ENTERED AT 14:43:36 ON 11 DEC 2002
L8           4 S L7

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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    19.45     319.96

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -2.48      -4.34

FILE 'REGISTRY' ENTERED AT 14:59:15 ON 11 DEC 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   10 DEC 2002  HIGHEST RN 475623-85-9
DICTIONARY FILE UPDATES:  10 DEC 2002  HIGHEST RN 475623-85-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L9      STRUCTURE UPLOADED

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L9              STR
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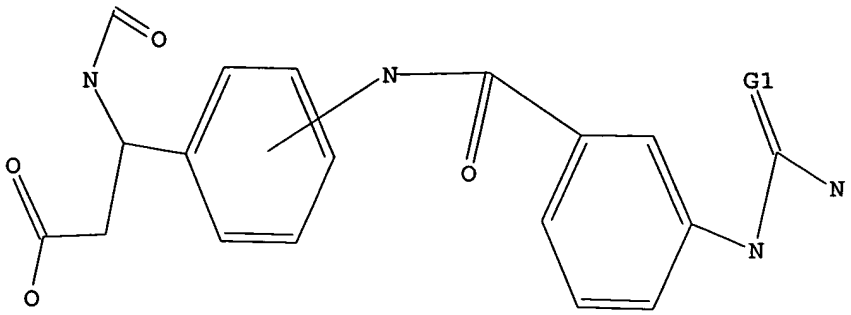

G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -     58 TO ITERATE

100.0% PROCESSED      58 ITERATIONS                                  0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          704 TO     1616
PROJECTED ANSWERS:               0 TO        0

L10           0 SEA SSS SAM L9

=> s l9 full
FULL SEARCH INITIATED 15:03:24 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   1026 TO ITERATE

100.0% PROCESSED    1026 ITERATIONS                                  0 ANSWERS
SEARCH TIME: 00.00.01

L11           0 SEA SSS FUL L9

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L12     STRUCTURE UPLOADED

=> d query
L12             STR
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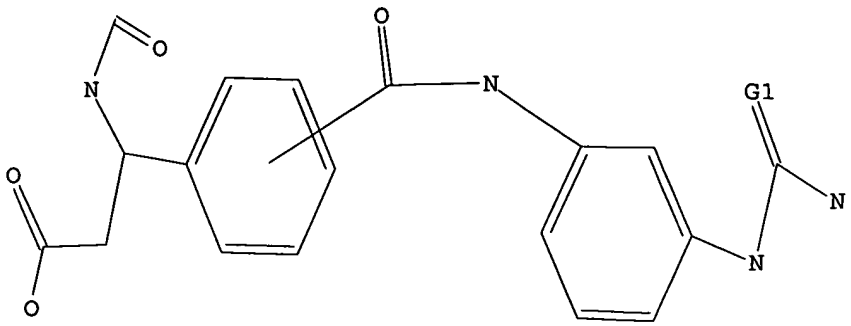

G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

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100.0% PROCESSED       2 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            2 TO      124
PROJECTED ANSWERS:               0 TO        0

L13           0 SEA SSS SAM L12

=> s l12 full
FULL SEARCH INITIATED 15:04:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     22 TO ITERATE

100.0% PROCESSED      22 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

L14           0 SEA SSS FUL L12

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L15     STRUCTURE UPLOADED

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L15             STR
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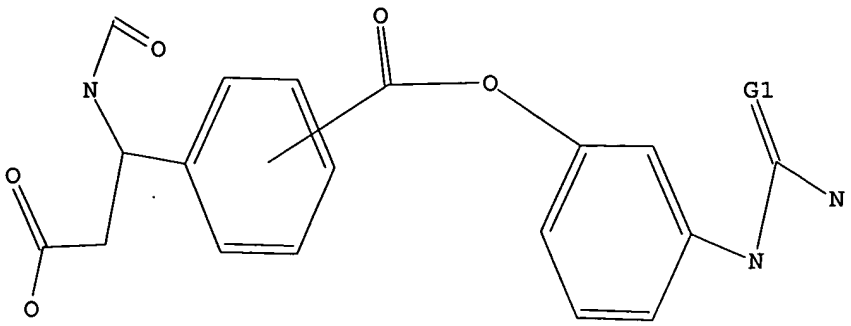

G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

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=> s l15
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SAMPLE SCREEN SEARCH COMPLETED -      1 TO ITERATE

100.0% PROCESSED       1 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            1 TO       80
PROJECTED ANSWERS:               0 TO        0

L16            0 SEA SSS SAM L15

=> s l15 full
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FULL SCREEN SEARCH COMPLETED -      7 TO ITERATE

100.0% PROCESSED       7 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

L17            0 SEA SSS FUL L15

=>
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L18     STRUCTURE UPLOADED

=> d query
L18             STR
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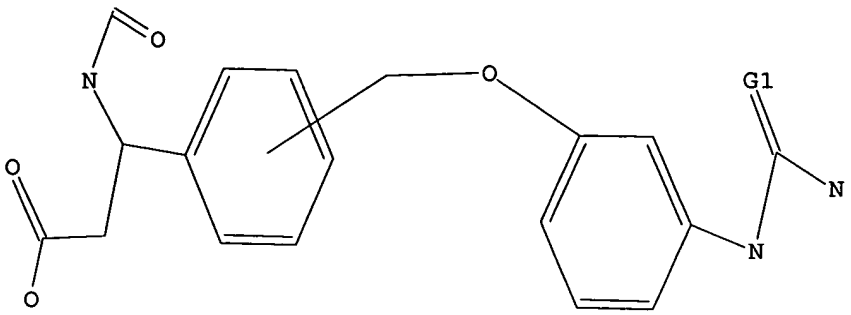

G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

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=> s l18
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100.0% PROCESSED        3 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            3 TO      163
PROJECTED ANSWERS:               0 TO        0

L19            0 SEA SSS SAM L18

=> s l18 full
FULL SEARCH INITIATED 15:05:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      24 TO ITERATE

100.0% PROCESSED       24 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L20            0 SEA SSS FUL L18

=>
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L21     STRUCTURE UPLOADED

=> d query
L21             STR
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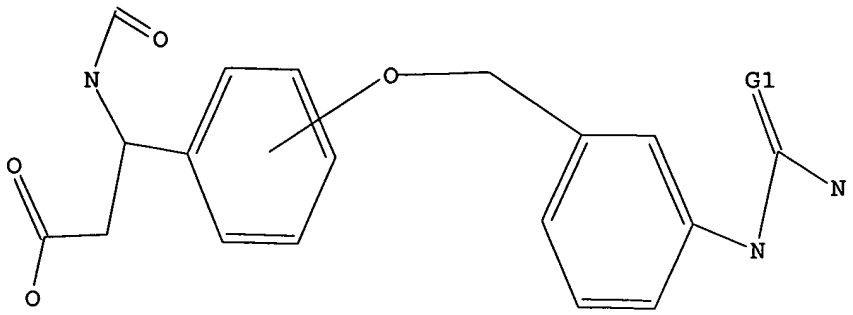

G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -     50 TO ITERATE

100.0% PROCESSED      50 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          576 TO     1424
PROJECTED ANSWERS:               0 TO        0

L22           0 SEA SSS SAM L21

=> s l21 full
FULL SEARCH INITIATED 15:06:32 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    910 TO ITERATE

100.0% PROCESSED     910 ITERATIONS                               0 ANSWERS
SEARCH TIME: 00.00.01

L23           0 SEA SSS FUL L21

=>
Uploading 09889455.str

L24     STRUCTURE UPLOADED

=>  d query
L24             STR
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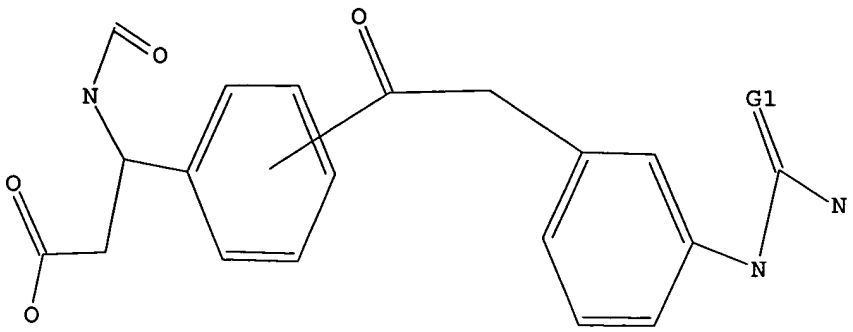

G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

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SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           22 TO      418
PROJECTED ANSWERS:               0 TO        0

L25           0 SEA SSS SAM L24

=> s l24 full
FULL SEARCH INITIATED 15:08:11 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    347 TO ITERATE

100.0% PROCESSED     347 ITERATIONS                               0 ANSWERS
SEARCH TIME: 00.00.01

L26           0 SEA SSS FUL L24

=>
Uploading 09889455.str

L27     STRUCTURE UPLOADED

=> d query
L27             STR
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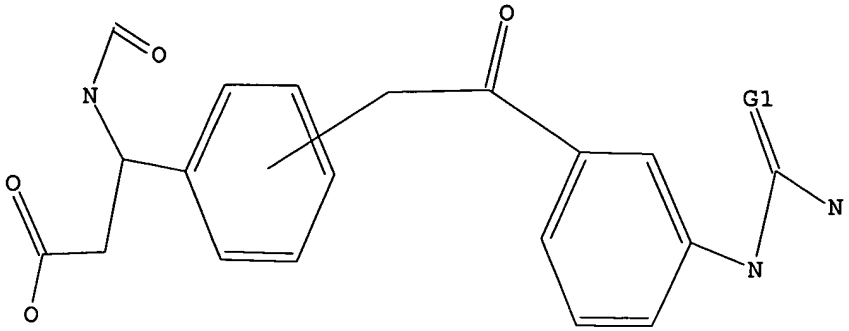

G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

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100.0% PROCESSED       0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   845.48    1165.44

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -4.34

STN INTERNATIONAL LOGOFF AT 15:09:01 ON 11 DEC 2002
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